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THE WILLIAM ALLAN MEMORIAL AWARD

Presented to Elizabeth F. Neufeld, Ph.D., at the annual meeting
of the American Society of Human Genetics
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Introduction by
KURT HIRSCHHORN[1]

SUMMARY

The opportunity for this presentation provides me with three gratifications. The first and most important is that the scientist being honored is Elizabeth Neufeld. The second is the honor bestowed upon me by being selected to introduce Dr. Neufeld. Finally, the preparation of this introduction has provided me with the opportunity to reconstruct a scientific career from its beginnings to its present exciting momentum, an exercise in which I was helped with great enthusiasm by a number of people who have known Liz during the various phases of her scientific life.

I am particularly pleased to note that our awardee is the product of that unique breeding ground of success stories, the special New York education system. After arriving in New York in 1940 at the age of 12 from Paris, a refugee from Nazi persecutions in Europe, Liz Neufeld, like so many other young refugees at the time, qualified for one of the specialized schools in New York—the Hunter College High School. From there she went to Queens College, one of the major high-quality free institutions of higher learning of the New York City college system, and graduated with a Bachelor of Science degree in 1948. Obviously turned on to a scientific career, she successfully applied for a research assistantship at the Jackson Laboratory in Bar Harbor, Maine, where she worked with the first of her mentors, Dr. Elizabeth Russell, to this day her good friend and enthusiastic admirer. Her first publications are derived from that experience and are concerned with hematologic genetics of mice. She then briefly went to the University of Rochester as a graduate student, an effort that was unfortunately interrupted for personal reasons. In 1951, she married Ben Neufeld, currently a health planner in the Health Resource Services Administration, and took a job as a research assistant with Nathan Kaplan, who at that time was doing his research at Johns Hopkins, and who was the second of her important early scientific influences. A

[1] Department of Pediatrics, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029.

series of papers resulted from this collaboration which concerns pyridine nucleotide metabolism. A year later she restarted her graduate education as a Ph.D. candidate with W. Z. Hassid in comparative biochemistry at Berkeley. During this highly productive phase of her life, she worked together with a number of people, among whom was Victor Ginsburg, who later was instrumental in pursuading DeWitt Stetten to bring her to the National Institutes of Health and to give her her own laboratory. Her work, resulting in numerous publications in the best biochemical journals, concentrated on nucleotides and complex carbohydrates, the latter providing her with the background for the experiments for which she is being honored today. She remained at Berkeley as a postdoctoral fellow with another important teacher, Dan Mazia, with whom she worked on nonprotein sulphydryl compounds in mitosis, acquainting her with an element of great importance in her future work. Following this fellowship, she returned to Hassid's laboratory, where she pursued a variety of directions concerning substituted sugars, polysaccharides, and glycoproteins. When, in 1963, despite her phenomenally productive research, there appeared to be a delay in obtaining a faculty position, at a time when recognition of leadership for women in science was still something of a novelty, she was brought to the National Institutes of Health, where she has been ever since. Her career blossomed, and she was promoted from research biochemist to Chief of the Section of Human Biochemical Genetics in 1973, and then in 1979, to Chief of the Genetics and Biochemistry Branch of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, the position which she holds at this time. She has been a member of a number of editorial boards and important committees and councils, including a term on the Board of Directors of this Society from 1977 to 1980. A major commitment has been her participation on the Board, and most recently as president of the Foundation for Advanced Education in the Sciences in Bethesda, an organization which helps foreign scientists to adjust, sponsors chamber music concerts, and provides an interface between science and culture for the National Institutes of Health community. She has received numerous honors during the last 10 years, including selection to the National Academy of Sciences in 1977, an honorary degree from the Rene Descartes University in Paris and Russell Sage College in 1980, and the prestigious Gairdner Foundation Award in 1981.

The specific work which has led to these well-deserved distinctions, as well as to the Allan Award, began in 1967, when Dr. Neufeld became interested in Hurler syndrome. It was accepted dogma in those days that mucopolysaccharides accumulated in this disease because of aberrant regulation of their synthesis resulting in overproduction. Her prior work on the biosynthesis of cell wall polymers in plants made her particularly qualified to study this problem, since such polymers share with mucopolysaccharides the presence of uronic acids or sugar nucleotides, a frequent theme in her earlier papers. She quickly saw the potential usefulness of cultured fibroblasts for such experiments in human biochemical genetics and began to tackle this problem. In those days, some of the best young people came to the National Institutes of Health as research associates to fulfill their term of military duty, and Liz was fortunate to be assigned one such associate, Joseph Fratantoni. She also had in her laboratory a prime example

of the type of people who can make or break a research effort, a superb technician in the form of Clara Hall, who has stayed with her as an active collaborator for all these years. When it became clear in their early work on Hurler cells that the current notions were not correct, they decided to study mucopolysaccharide turnover in the cells by incorporating radioactive sulfate into newly synthesized mucopolysaccharides and studying their degradation with chase experiments. These studies, in part, became possible because of her development of a simplified assay technique involving the specific precipitation of these molecules by boiling in 80% ethanol, a method derived from her own early work. She quickly showed that the defect in the Hurler syndrome was due to decreased degradation of the molecules and their resulting accumulation in lysosomes. This work resulted in an important paper by Fratantoni, Hall, and Neufeld published in the *Proceedings of the National Academy of Sciences* in 1968. This work was followed by one of the most exciting experiments in human genetics. Dr. Neufeld was puzzled by the observation that women heterozygous for the X-linked Hunter syndrome, another mucopolysaccharidosis, did not show any clinical symptoms despite the fact that the Lyon hypothesis would have predicted that about half the cells in such women should be abnormal. She discussed this problem during a visit from her earlier tutor, Elizabeth Russell, and postulated that a fibroblast culture made up of a mixture between cells from a patient with Hunter syndrome and from a normal male might be a good model for the study of this problem. This experiment was not done. However, soon thereafter, Fratantoni inadvertently mixed cells from a Hurler patient with those from a Hunter patient in the same culture vessel. Remembering the experiment proposed by Dr. Neufeld, he told her of this lucky mishap, and they decided to do their sulfate incorporation experiments in the mixture. The rest is history. The mixture behaved in essence like normal cells. The classic publication in *Science* in 1968, demonstrating the cross-correction between the two cell types, led to a vast amount of work in her laboratory as well as in many others. It allowed for the elucidation of the specific enzyme defects in all of the mucopolysaccharidoses, it permitted an accurate classification of these diseases, it provided for one of the clearest examples of genetic heterogeneity in man, it has led to proposed strategies for enzyme replacement therapy, it opened the door to an understanding of the interaction of enzymes with cell surface receptors, and it provided the background for the current exciting activity in Dr. Neufeld's and other laboratories relating to the normal processing of lysosomal enzymes and related molecules as well as abnormalities of such processing. A large number of publications followed over the next 14 years, written with numerous scientists working in her laboratory. Each of these papers has given further evidence of what was recognized by Dr. Neufeld's early supervisors: her super technical abilities, her unshakable persistence in the pursuit of a research problem to its logical conclusion, and, above all, her imaginative creativity and insight into fundamental biological phenomena. Her most recent papers have reported an esthetically beautiful series of experiments involving the detailed dissection of the synthesis, processing, and transport of lysosomal enzymes in normals and abnormals, which are certain to lead to a clear understanding of a critical component of cell biology.

During this exemplary productive career, Liz and Ben Neufeld have produced and developed a family, their son Ellis, currently an M.D./Ph.D. student at Washington University in St. Louis, and their daughter Sophie, who works with horses as expertly as her mother does with molecules and cells. Her family, on the one hand, and the human genetics community, on the other, owe great debts to Liz Neufeld. It is with great appreciation and respect that I present to the Society Dr. Elizabeth Neufeld as the recipient of the William Allan Memorial Award.

Erratum

In the paper "Patterns of DNA Replication of Human Chromosomes. II. Replication Map and Replication Model," by M. Camargo and J. Cervenka (*Am J Hum Genet* 34:757–780, 1982), the legend for figure 2 (page 762) should be replaced by the legend under figure 3 (page 765) and vice versa. Also, chromosomes (photos) and idiograms for chromosomes 6, 7, and 8 in figure 4, page 769, were numbered incorrectly and should be corrected as below. Correction regarding these three chromosomes also applies to figure 1.